

Amendments to the Specification

Amend the specification at page 2, lines 13-18 as follows:

Above all in the treatment of ~~chronic~~ chronic diseases, which in the majority of cases involve elderly patients, the pharmaceutical forms and the embodiments described above have the undoubted advantage of allowing a drastic simplification of the dosage schemes with administrations which, in many cases, can be reduced to once a day, obtaining in addition a greater observance (compliance) by the patient of the prescribed therapy.

Amend the specification at page 5, lines 3-4 as follows:

~~Figure 2~~ Figure 3: cross sectional view of the tablet in Figure 1, showing two incisions (5) on the faces of the coating.

Amend the specification at page 10, lines 10-21 as follows:

The polymeric substances of the barrier layer can be selected, for example, from the group consisting of hydroxypropylmethylcellulose with molecular weight ranging between 1000 and 4000000, hydroxypropylcellulose with molecular weights ranging between 2000 and 2000000, polyoxyethylenes (PEO POE) with molecular weights ranging between 1000 and 10000000, carboxyvinyl polymers, polyvinyl alcohols with molecular weights ranging between 10000 and 1000000, polyamides, polyanhydrides, polyvinylpyrrolidone, glucans, scleroglucans, mannans, xanthans, carragenans, galactomannans, gellans, polyaminoacids, poly (methyl vinyl ethers/maleic anhydride), carboxymethylcellulose and derivatives, ethylcellulose, methylcellulose, cellulose derivatives in general, alginic acid and salts and derivatives thereof, starches, starch derivatives, α -, β -, γ - ~~cyclodextrins~~ cyclodextrins and copolymers of the above mentioned polymers.

Amend the specification at page 12, line 32 through page 13, line 1 as follows:

The thickness of the coating film may range from 5 to 1000 μm ~~μm~~ but preferably from 20 to 500 μm ~~μm~~ .

Amend the specification at page 13, line 30 through page 14, line 14 as follows:

Amongst the active substances of possible use in the present system can be listed all the active substances able to carry out their curative and/or protective action towards and in particular to circadian rhythms, for example : non steroid anti inflammatory substances (NSAID) such as sodium diclofenac ~~dielephenae~~, indomethacin, ibuprofen, ketoprofen, diflunisal, pyroxicam, naproxene, flurbiprofen, sodium tolmetin, paracetamol, anti inflammatory steroids or sleep inducing substances and tranquillisers such as diazepam, nitrazepam, flurazepam, oxazepam, chlordiazepoxide, medazepam, lorazepam, active ingredients for the control of hypertension such as amlodipine, captopril, clonidine, diltiazem, enalapril, felodipine, katanerine, lisinopril, methyldopa, nifedipine, nitrendipine, nicardipine, prazosine, ramipril, beta blockers such as atenolol, metoprolol, pindolol, propanolol, timolol, diuretics such as amiloride, clortalidone, frusemide, hydrochlorotiazide, indapamide, spironolattone, anti Parkinson's drugs such as amantidine, bromocriptin, levodopa, antihistamines such as tripelennamine, terfenadine, anti asthmatics such as ketothiophene, nedocromil, antibiotics alone and in association or chemotherapeutic agents.

Amend the specification at page 15, line 31 as follows:

Total Totale 100%

Amend the specification at page 15, line 32 through page 16, line 7 as follows:

The envisaged amount of hydroxypropylmethylcellulose and hydrogenated castor oil are mixed, in an appropriate mixer, with the blue laquer colouring; the homogeneous mixture obtained, lightly blue coloured, is humidified in a hydro- alcoholic solution of 10% polyvinylpyrrolidone. The uniformly humid mass is forced through a 25 mesh grille (equal to 710 µm ~~mm~~) obtaining a granulate which is dried in a hot air circulating oven until constant weight. The dried granulate, re-calibrated through the same grid, is added with magnesium stearate and colloidal silicate.

Amend the specification at page 17, lines 8-12 as follows:

The filming operation is carried out in a traditional stainless steel basin 30 cm in diameter; the solution of the polymeric coating material is sprayed with a traditional air jet system (Asturo

Mec type with nozzles from 1.0 mm). The filming operation is carried out until the application of a continuous, homogeneous and regular coating film is achieved for each tablet with a thickness of approx. 100 μm .

Amend the specification at page 17, lines 24-26 as follows:

The incision is carried out in a time of around 100 milliseconds, an application necessary and sufficient to perforate the coating film of a thickness of about 100 μm .

Amend the specification at page 19, lines 9-11 as follows:

The incision is performed in a time of around 100 milliseconds, the application necessary and sufficient to perforate the coating film with a thickness of approx. 100 μm .

Amend the specification at page 20, lines 27-29 as follows:

The incision is performed in a time of around 100 milliseconds, the application necessary and sufficient to perforate the coating film of a thickness of approx. 100 μm .

Amend the specification at page 22, lines 14-21 as follows:

The envisaged amount of diltiazem is mixed, in a appropriate mixer, with the lactose and the corn starch; the homogeneous mixture obtained is humidified with an aqueous solution of 1.3% methylcellulose in water. The uniformly humid mass is forced through a 25 mesh grid (equal to 710 μm) obtaining a granulate which is dried in a hot air circulating oven until constant weight. The dried granulate, recalibrated through the same grille, is added to the disaggregants, the magnesium stearate and the colloidal silicate. The mass is mixed in a V shaped mixer for 30 minutes.

Amend the specification at page 23, lines 2-9 as follows:

The envisaged amount of hydroxypropylmethylcellulose and of hydrogenated castor oil is mixed, in an appropriate mixer, with the green coloured laquer ; the homogeneous mixture

obtained, lightly green in colour, is humidified with an hydroalcoholic solution of 10% Polyvinylpyrrolidone. The uniformly humidified mass is forced through a 25 mesh grid (equal to 710 μm $\ominus\text{m}$) obtaining a granulate which is dried in a hot air circulation oven until constant weight. The dried granulate, re-calibrated through the same grille, is added to the stearic acid. The mass is mixed in a V shaped mixer for 30 minutes.

Amend the specification at page 24, lines 26-28 as follows:

The incision is performed in a time of around 100 milliseconds, such application necessary and sufficient to perforate the coating film of a thickness of around 100 μm $\ominus\text{m}$.

Amend the specification at page 25, lines 27-29 as follows:

Example 5: The preparation of a series of 5000 three layered tablets as reported in Fig. 3, comprising such active ingredient in the first layer 50 mg of hydrochlorothiazide, in the third layer 80 mg of pf propanolol and a barrier layer.

Amend the specification at page 26, lines 8-15 as follows:

The envisaged amount of hydrochlorothiazide is mixed, in appropriate mixer, with hydroxypropylmethylcellulose and lactose; the homogeneous mixture obtained is humidified with an aqueous solution of 1.3% methylcellulose in water. The uniformly humidified mass is forced through a 25 mesh grid (equal to 710 μm $\ominus\text{m}$) obtaining a granulate which is dried in a hot air circulating oven until constant weight. The dried granulate, re-calibrated through the same grid, is added to the magnesium stearate and the colloidal silica. The mass is mixed in a V shaped mixer for 30 minutes.

Amend the specification at page 26, line 29 through page 27, line 4 as follows:

The envisaged amount of propanolol is mixed, in appropriate mixer, with hydroxypropylmethylcellulose and lactose and blue laquer ; the homogeneous mixture obtained, lightly green in colour, is humidified with an aqueous solution of 1.3% methylcellulose in water. The uniformly humid mass is forced through a 25 mesh grid (equal to 710 μm $\ominus\text{m}$) obtaining a

granulate which is dried in a hot air circulating oven until constant weight. The dried granulate, re-calibrated through the same grille, is added to the magnesium stearate and the colloidal silica. The mass is mixed in a V shaped mixture for 30 minutes.

Amend the specification at page 27, lines 18-25 as follows:

The envisaged amount of hydroxypropylmethylcellulose and hydrogenated castor oil are mixed, in an appropriate mixer, with the orange coloured laquer ; the homogeneous mixture obtained, lightly coloured, is humidified with a hydroalcoholic solution of 10% polyvinylpyrrolidone. The uniformly humidified mass is forced through a 25 mesh grid (equal to 710 μm \pm m) obtaining a granulate which is dried in a hot air circulating oven to constant weight. The dried granulate, re-calibrated through the same grille, is added to the stearic acid. The mass is mixed in a V shaped mixer for 30 minutes.

Amend the specification at page 29, lines 1-3 as follows:

The incisions are carried out in a time of approx. 100 milliseconds, the application necessary and sufficient to perforate the coating film with a thickness of approx. 100 μm \pm m.

Amend the specification at page 30, lines 18-20 as follows:

The incision is carried out in a time of approx. 100 milliseconds, the application necessary and sufficient to perforate the coating film with a thickness of approx. 100 μm \pm m.